Hg (0.1%), as compared to baseline measurements. After topical application of 8-iso PGE_2 the IOP was lower ($p<0.01$) in the treated eyes of 6 N monkeys for 4 hrs, with a maximum difference of 3.2±0.2 mmHg, as compared to the fellow contralateral control eyes. The pupil size was smaller ($p<0.01$) for 4 hrs, up to 1.0±0.2 mm. Compared with vehicle-treated contralateral control eyes, C was greater ($p<0.005$) by 48% at 2 hr after a single dose of 0.1% 8-iso PGE_2. F was unchanged ($p<0.10$) over a period of 4 hrs after drug administration. Mild eyelid edema, conjunctival edema, hyperemia, and discharge appeared in some eyes treated with the 0.1% concentration.

Table 1A shows that 8-iso PGE_2 administered to the normal monkey eye lowers IOP significantly by 20.3% and increases outflow facility by 43.1%, an amount sufficient to account for the fall of IOP. By contrast, in Table 1B latanoprost in the normal monkey eye also lowers IOP significantly (by 10.8%), but the drug has no significant effect on outflow facility. The lack of a major effect on outflow facility of latanoprost in the primate eye is in agreement with studies in the literature by other investigators.

TABLE 1

A. Effect of 0.1% 8-isoPGE_2 on Outflow Facility in 6 Normal Monkeys (2 hours after treatment)

	Intraocular Pressure Mean ± SEM mmHg	Outflow Facility Mean ± SEM μl/ml/mmHg
Treated eyes (drug)	13.0 ± 0.7*	0.83 ± 0.10*
Baseline	16.3 ± 1.1	0.58 ± 0.03
Control eyes (vehicle)	15.7 ± 0.5	0.56 ± 0.06
Baseline**	15.7 ± 0.6	0.51 ± 0.04

B. Effect of 0.005% latanoprost on Outflow Facility in 6 Normal Monkeys (1 hour after treatment)

	Intraocular Pressure Mean ± SEM mmHg	Outflow Facility Mean ± SEM μl/min/mmHg
Treated eyes (drug)	13.2 ± 0.7*	0.76 ± 0.08
Baseline	14.8 ± 0.7	0.62 ± 0.07
Control eyes (vehicle)	15.0 ± 0.8	0.60 ± 0.07
Baseline**	15.7 ± 0.3	0.73 ± 0.08

*Significantly different as compared with either baseline values or vehicle-treated eyes (two-tailed paired t-test, p. < 0.05.
**Baseline measurements made in the same monkeys at the same time one day prior to drug treatments

Table 2 shows the effect of 8-iso PGE_2 on IOP and outflow facility in glaucomatous monkey eyes. Because of the individual variability in laser-induced glaucomatous monkey eyes, the IOP and facility measurements are expressed in the table as ratios (value of the drug-treated eye÷the value of the vehicle-treated eye). The ratios were calculated from the values of the same glaucomatous monkey eye determined immediately prior to administration of the drug or the vehicle (time 0 hrs.), and the values at 2 hours after administration of the drug or vehicle. The data in Table 2 show that in the primate, administration of 8-iso PGE_2 to glaucomatous eyes significantly lowers IOP (by 13.8%) and significantly increases outflow facility (by 38.8%), which is of sufficient magnitude to account for the fall in IOP. Thus the mechanism of lowering IOP by 8-iso PGE_2 in both normal and glaucomatous eyes is primarily due to an increase in aqueous humor trabecular outflow.

TABLE 2

Effect of 0.1% 8-iso PGE_2 on IOP and Outflow Facility Responses in 8 Glaucomatous Monkey Eyes (Unilateral)

	Intraocular Pressure (drug-treated/ vehicle-treated)		Outflow facility (drug-treated/ vehicle treated)	
Time	0 hr	2 hr	0 hr	2 hr
Response Ratio (± SEM)	0.976 ± 0.002	0.843* ± 0.0498	1.041 ± 0.0498	1.445** ± 0.161
% Change by drug	—	13.8% decrease	—	38.8% decrease

Significantly different as compared to 0 hr, paired t-test, p < 0.01*, <0.10**

EXAMPLE II

IOP was measured one hour before and at intervals up to six hours after a single dose of 8-iso PGE, (the 13, 14 dihydro derivative of 8-iso PGE_2), 8-iso PGE_2, or 8-iso $PGF_{2\alpha}$ in laser-induced glaucomatous eyes in cynomolgus monkeys (wherein only one eye is rendered glaucomatous and the other serves as a control). Following one day of baseline IOP measurement, a single 25 μl dose of either (i) 0.1 percent 8-iso PGE_1, or (ii) 0.1 percent 8-iso PGE_2, or (iii) 0.1 percent 8-iso $PGF_{2\alpha}$, was topically applied to the glaucomatous eye in groups of 4 or 8 monkeys. It was found that 8-iso PGE_1 (0.1 percent) reduced IOP ($p<0.05$) for up to four hours in glaucomatous monkey eyes (n=4). The maximum reduction in IOP was 5.3±0.8 (mean±SEM) mm Hg at 2 hours after dosing. 8-iso PGE_2 (0.1 percent) reduced IOP ($p<0.05$) for 5 hours with a maximum reduction in IOP of 6.6±0.8 mm Hg at 2 hours after dosing (n=8). After 0.1 percent 8-iso $PGF_{2\alpha}$, a significant ($p<0.05$) reduction in IOP occurred only at 1 hour with the maximum reduction in IOP of 3.3±0.9 mm Hg (n=4). The results are shown in Table 3. Based on these studies, of the compounds tested, 8-iso PGE_2 appears to have the greatest and 8-iso $PGF_{2\alpha}$. the least activity in decreasing IOP in glaucomatous monkey eyes.

TABLE 3

Intraocular Pressure (treated - baseline) (mean mm Hg ± SEM)

iso PG, 0.1%	n	1 hr	2 hr	4 hr	6 hr
8-iso PGE_1	4	−3.3 ± 1.3	−5.3 ± 0.8*	−2.3 ± 0.5*	−1.3 ± 0.9
8-iso PGE_2	8	−4.5 ± 0.9**	−6.6 ± 0.8**	−2.9 ± 0.6**	−1.2 ± 1.2
8-iso $PGF_{2\alpha}$	4	−3.3 ± 0.8*	−1.8 ± 1.1	−0.8 ± 1.7	0.3 ± 0.5

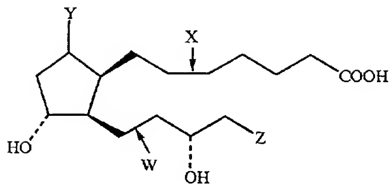
*p < 0.05
**p < 0.005

Various publications are cited herein, the contents of which are hereby incorporated by reference in their entireties.

We claim:

1. A method for decreasing intraocular pressure comprising administering a therapeutically effective amount of an 8-iso prostanoid having the following Formula I:

Formula I



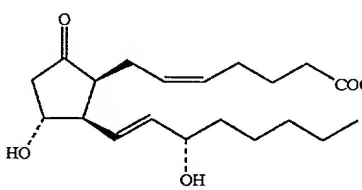
where bond W is selected from the group consisting of a single covalent bond and a double covalent bond, bond X is selected from the group consisting of a single covalent bond and a double covalent bond, substituent Y is selected from the group consisting of a hydroxyl group having either α or β orientation relative to the five-membered ring and a keto function, and substituent Z is a hydrocarbon group selected from the group of aliphatic, aromatic, or a combination of aliphatic and aromatic hydrocarbon, to a patient in need of such treatment.

2. The method of claim 1 wherein the 8-isoprostanoid is administered topically.

3. The method of claim 2 wherein the 8-iso prostanoid is administered as a composition comprising between 0.005 to 1 percent 8-iso prostanoid.

4. The method of claim 1, wherein the 8-iso prostanoid is selected from the group consisting of a compound having the following Formula II

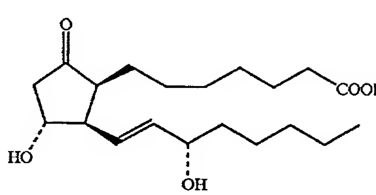
Formula II



or a derivative thereof.

5. The method of claim 1, wherein the 8-iso prostanoid is selected from the group consisting of a compound having the following Formula III

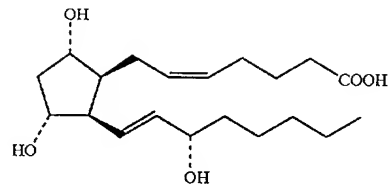
Formula III



or a derivative thereof.

6. The method of claim 1, wherein the 8-iso prostanoid is selected from the group consisting of a compound having the following Formula IV

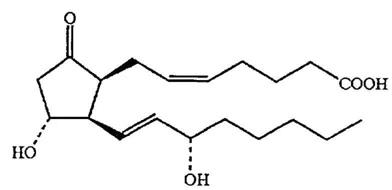
Formula IV



or a derivative thereof.

7. The method of claim 2, wherein the 8-iso prostanoid is selected from the group consisting of a compound having the following Formula II

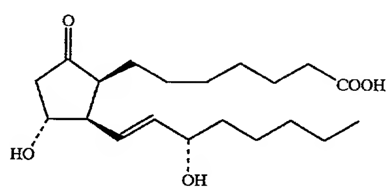
Formula II



or a derivative thereof.

8. The method of claim 2, wherein the 8-iso prostanoid is selected from the group consisting of a compound having the following Formula III

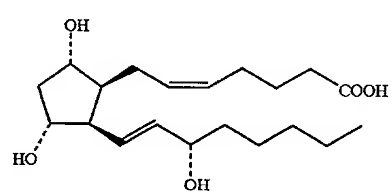
Formula III



or a derivative thereof.

9. The method of claim 2, wherein the 8-iso prostanoid is selected from the group consisting of a compound having the following Formula IV

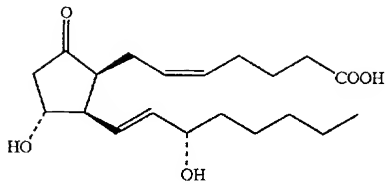
Formula IV



or a derivative thereof.

10. The method of claim 3, wherein the 8-iso prostanoid is selected from the group consisting of a compound having the following Formula II

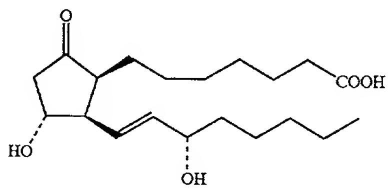
Formula II



or a derivative thereof.

11. The method of claim 3, wherein the 8-iso prostanoid is selected from the group consisting of a compound having the following Formula III

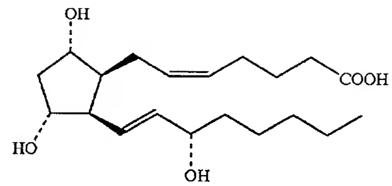
Formula III



or a derivative thereof.

12. The method of claim 3, wherein the 8-iso prostanoid is selected from the group consisting of a compound having the following Formula IV

Formula IV



or a derivative thereof.

13. The method of claim 4, wherein the derivative is an ester derivative.

14. The method of claim 5, wherein the derivative is an ester derivative.

15. The method of claim 6, wherein the derivative is an ester derivative.

16. The method of claim 7, wherein the derivative is an ester derivative.

17. The method of claim 8, wherein the derivative is an ester derivative.

18. The method of claim 9, wherein the derivative is an ester derivative.

19. The method of claim 10, wherein the derivative is an ester derivative.

20. The method of claim 11, wherein the derivative is an ester derivative.

21. The method of claim 12, wherein the derivative is an ester derivative.

* * * * *